Cancer Immunology Immunotherapy (CANCER IMMUNOL. IMMUNOTHER.) (Germany) 1995, 40/6 (383-389)
CODEN: CIIMD ISSN: 0340-7004
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LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

The transfer of human peripheral blood mononuclear cells (hu-PBMC) from adult Epstein-Barr-virus(EBV)-seropositive donors in SCID (severe combined immunodeficiency) mice frequently leads to the development of a human B lymphoproliferative syndrome (hu-BLPS). Therefore, as 90% of adult potential donors are EBV-seropositive, efforts have to be made to avoid the occurrence of this B lymphoproliferative disorder. McCune et al. (Science 241:1632 (1988)) used human fetal organs for a human SCID graft. This system does not give rise to hu-BLPS but human fetal organs are much less available than peripheral blood leucocytes. The experiments reported in this paper show how crucial is the presence of functional T lymphocytes for a graft to take and for development of hu-BLPS in hu-PBMC-reconstituted SCID mice, since inhibition of T lymphocyte by a rat anti-(human CD2) monoclonal antibody (**LO - CD2a**) during the first 10 days of the graft prevents successful engraftment of human normal lymphocytes as well as hu-BLPS in SCID mice. The transfer of B cells alone or B cells plus monocytes in SCID mice does not permit either long-term engraftment or development of hu-BLPS. We also demonstrate that hu-PBMC treated with L-leucine methyl ester are less susceptible to the development of hu-BLPS after engraftment in SCID mice than are untreated hu-PBMC. The mechanism of action of L-leucine methyl ester on these cells is discussed.

Set	Items	Description
S1	40	(BTI(W)322) OR BTI322
S2	19	RD (unique items)
S3	1	S2 NOT PY>1995
S4	30	LO(W)CD2A
S5	18	RD (unique items)
S6	10	S5 NOT S2

The influence of cyclosporin A on the alternative pathways of human T cell activation in vitro.

Bloemena E; Van Oers R H; Weinreich S; Stilma-Meinesz A P; Schellekens P T; Van Lier R A
Central Laboratory of the Netherlands Red Cross Blood Transfusion Service, Amsterdam.

European journal of immunology (GERMANY, WEST) May 1989, 19 (5) p943-6, ISSN 0014-2980 Journal Code: 1273201
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

To gain further insight into the mechanism of action of the immunosuppressant **cyclosporin** A (CyA), we investigated the influence of CyA on proliferative responses of human T lymphocytes, induced via different membrane molecules. As was previously shown, activation of T cells via the T cell receptor (Ti)/CD3 complex with an anti-CD3 monoclonal antibody was inhibited by CyA. Likewise, triggering of T lymphocytes via the alternative, **CD2** (T11)-mediated pathway of activation was strongly inhibited. In contrast, responses induced by phorbol myristate 13-acetate (PMA; 100 ng/ml) or the combination of an anti-CD28 monoclonal antibody and a suboptimal concentration of PMA (1 ng/ml) were found to be insensitive to CyA. CyA-induced inhibition of both anti-CD3- and **anti - CD2** -mediated proliferation could not be reversed by addition of either PMA (1 ng/ml) or anti-CD28. An increase in the intracellular free Ca2+ concentration [(Ca2+]i) is an early event observed after stimulation of T cells via CD3 or **CD2** , whereas stimulation with PMA and anti-CD28 does not lead to a rise in [Ca2+]i. This suggests that the inhibitory action of CyA is related to Ca2+-dependent signaling pathways. Since we observed that CyA does not interfere with anti-CD3- or **anti - CD2** -induced increases of [Ca2+]i, our data suggest that CyA-mediated inhibition is related to a later event in these intracellular signaling pathways.

Human marrow T cell dose correlates with severity of subsequent acute

graft-versus-host disease.
Atkinson K; Farrelly H; Cooley M; O'Flaherty E; Downs K; Biggs J
Department of Haematology, St Vincent's Hospital, Sydney, Australia.
Bone marrow transplantation (ENGLAND) Jun 1987, 2 (1) p51-7, ISSN 0268-3369 Journal Code: 8702459
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Sixteen patients with haematological malignancy received high-dose chemotherapy or chemotherapy and total body irradiation followed by an HLA-identical sibling marrow transplant from which the T lymphocytes had been depleted prior to infusion by incubation with an **anti - CD2** anti-T cell antibody with (seven patients) or without (nine patients) an anti-CD8 anti-T cell antibody together with rabbit complement. Additionally, all patients received **cyclosporin** . The number of T cells present in the donor marrow was determined by limiting dilution analysis, and was found to correlate with the subsequent incidence and severity of acute graft-versus-host disease (GVHD). The number of T cells infused into patients with no acute GVHD or with minimal acute GVHD of the skin (skin rash present for 14 days or less) was 1.3 +/- 1.0 x 10(5)/kg, while the number infused into those with moderate acute GVHD or with skin acute GVHD present for 15 days or more was 12.3 +/- 11.5 x 10(5)/kg (p less than 0.001). Thus a dose of 10(5) (or less) T cells/kg was associated with minimal or no acute GVHD, while 10(6) T cells/kg (or more) caused significant disease.**Title: CD2-MEDIATED AUTOCRINE GROWTH OF HERPES-VIRUS SAIMIRI-TRANSFORM HUMAN LYMPHOCYTES-T** (Abstract Available)
Author(s): MITTRUCKER HW; MULLERFLECKENSTEIN I; FLECKENSTEIN B; FLEISCHER B
Corporate Source: UNIV MAINZ,DEPT MED 1,LANGENBECKSTR 1/W-6500 MAINZ//GERMANY/; UNIV MAINZ,DEPT MED 1,LANGENBECKSTR 1/W-6500 MAINZ//GERMANY/; UNIV ERLANGEN NURNBERG,INST CLIN & MOLEC VIROL/W-8520 ERLANGEN//GERMANY/
Journal: JOURNAL OF EXPERIMENTAL MEDICINE, 1992, V176, N3 (SEP 1), P909-913
ISSN: 0022-1007
Language: ENGLISH Document Type: NOTE
Abstract: Herpes virus saimiri (HVS) immortalizes T lymphocytes from a variety of primates and causes acute T cell lymphomas and leukemias in nonnatural primate hosts. Here we have analyzed the requirements for growth of three HVS-transformed human T cell lines. The cells expressed the phenotype of activated T cells: two were CD4+, and one was CD8+. All three cells responded to all allogeneic human cell lines tested with enhanced proliferation, production of interleukin 2 (IL-2), and increased expression of the IL-2 receptor. Binding of **CD2** to its ligand CD58 was the critical event mediating stimulation because: (a) monoclonal antibodies (mAbs) to **CD2** and to CD58, but not to a variety of other surface structures, blocked induced and spontaneous proliferation and IL-2 production; (b) only **anti - CD2** mAbs were stimulatory if crosslinked; (c) a nonstimulatory cell was rendered stimulatory by CD58 transfection; and (d) the cells responded specifically to CD58 on sheep red blood cells. Growth of the cells required activation because **cyclosporin** A and **FK506** blocked stimulator cell-induced IL-2 production and proliferation as well as the spontaneous growth of the lines. Antibodies to the IL-2 receptor reduced proliferation of the cells and blocked IL-2 utilization. Taken together, these results show that HVS-transformed T cells proliferate in response to **CD2** -mediated contact with stimulator cells or with each other in an IL-2-dependent fashion. They suggest that HVS transforms humanSet Items Description

S1	40	(BTI(W)322) OR BTI322
S2	19	RD (unique items)
S3	1	S2 NOT PY>1995
S4	30	LO(W)CD2A
S5	18	RD (unique items)
S6	10	S5 NOT S2
S7	357	CD2 (S) (RAPAMYCIN OR CYCLOSPORIN OR CYSA OR FK506)
S8	62	S7 AND (ANTI(W)CD2)
S9	17	RD (unique items)
S10	12	S9 NOT PY>1995

Potent apoptotic signaling and subsequent unresponsiveness induced by a single CD2 mAb (BTI - 322) in activated human peripheral T cells.

Dumont C; Deas O; Mollereau B; Hebib C; Giovino-Barry V; Bernard A; Hirsch F; Charpentier B; Senik A

Centre National de Recherche Scientifique, UPR 420, Villejuif, France.

Journal of immunology (Baltimore, Md. : 1950) (UNITED STATES) Apr 15 1998, 160 (8) p3797-804, ISSN 0022-1767 Journal Code: 2985117R

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Manipulation of CD2 molecules with CD2 mAb pairs has been shown to deliver apoptotic signals to activated mature T cells. We show that **BTI - 322** , a CD2 mAb directed at a peculiar epitope of CD2, can trigger on its own the apoptotic death of IL-2-activated peripheral T cells and of OKT3-stimulated T cells, contrasting in this respect with a series of other mouse or rat CD2 mAb. F(ab')2 fragments were as potent as the whole Ab. **BTI - 322** -induced apoptosis proceeded in a few hours and was independent of the Fas/Fas ligand system. Less than 5 ng/ml of **BTI - 322** , adde**Title: The use of t 322)in adult liver transplantation (LT) preliminary results of a prospective randomized study**

Author(s): Lerut JP; Laterre PF; Ciccarelli O; Roggen F; Fraipont B; Talpe S; Sempoux C; Gianello P; Otte JB; Hope J; Bazin H; Latinne D

Corporate Source: CATHOLIC UNIV LOUVAIN,DEPT DIGEST SURG/BRUSSELS//BELGIUM/ ; CATHOLIC UNIV LOUVAIN,DEPT DIGEST SURG/BRUSSELS//BELGIUM/; CATHOLIC UNIV LOUVAIN,DEPT INTENS CARE/BRUSSELS//BELGIUM/; CATHOLIC UNIV LOUVAIN,DEPT PATHOL/BRUSSELS//BELGIUM/; CATHOLIC UNIV LOUVAIN,LABS EXPT SURG/BRUSSELS//BELGIUM/; CATHOLIC UNIV LOUVAIN,IMMUNOL LAB/BRUSSELS//BELGIUM/; BIOTRANSPLANT,/BOSTON//MA/

Journal: TRANSPLANTATION, 1999, V67, N7 (APR 15), P102-102

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Language: English Document Type: MEETING ABSTRACT

An anti-CD2 monoclonal antibody that elicits alloantigen-specific hyporesponsiveness

Schad V.; Greenstein J.L.; Giovino-Barry V.; LeGuern A.; Matejic T.; Glaser R.; Dickerson M.; Xu Y.; Bazin H.; Latinne D.; Monroy R.; White-Scharf M.E.

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Transplantation Proceedings (TRANSPLANT. PROC.) (United States) 1996, 28/4 (2051-2053)

CODEN: TRPPA ISSN: 0041-1345

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LANGUAGE: ENGLISH

ESOT update on immunosuppressive substances in clinical development or use 1995

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Transplant International (TRANSPLANT INT.) (Germany) 1996, 9/3 (171-174)

CODEN: TRINE ISSN: 0934-0874

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The ESOT Council conducted an inquiry on new immunosuppressive substances in order to help keep members of ESOT informed. Thirty-one pharmaceutical companies were sent a questionnaire indicating whether they were developing new immunosuppressive substances/antibodies. Sixteen companies responded: 11 furnished information on 16 substances; 5 said that they were not developing any new immunosuppressive agents. Fifteen companies did not reply at all. The results of the first inquiry are reported here.

A rat monoclonal anti-(human CD2) and L-leucine methyl ester impacts an human/SCID mouse graft and B lymphoproliferative syndrome

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